UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,372	08/15/2002	Gilles Pitiot	065691-0270	1002

22428 7590 07/06/2005

FOLEY AND LARDNER
SUITE 500
3000 K STREET NW
WASHINGTON, DC 20007

EXAMINER	
ULM, JOHN D	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 07/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,372	PITIOT ET AL.	
	Examiner	Art Unit	
	John D. Ulm	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *23 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-9 and 11* is/are rejected.

7)☒ Claim(s) *5,6,10,12-22,24-45 and 47-51* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/13/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1) Claims 1 to 51 are pending in the instant application.

2) Claim 4 does not comply with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification and claims wherever a reference is made to that sequence. Correction is required. See M.P.E.P. 2422.03.

3) Claims 5, 6, 10, 12 to 22, 24 to 45 and 47 to 51 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from another multiple dependant claim. See MPEP § 608.01(n). Accordingly, these claims have not been further treated on the merits.

4) Claims 23 and 46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 24 May of 2005.

5) Claims 1 to 4 and 7 to 11 are objected to as reciting an improper Markush Group. M.P.E.P. 803.02 states that:

> "Since the decisions in In re Weber **,198 USPQ 328 (CCPA 1978); and In re Haas, 198 USPQ 334 (CCPA 1978), it is improper for the Office to refuse to examine that which applicants regard as their invention, unless the subject matter in a claim lacks unity of invention, In re Hamish , 631 F.2d 716, 206 USPQ 300 (CCPA 1980); Ex Parte Hozumi , 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility."

The six different amino acid sequences recited in these claims, and the nucleotide sequences encoding them, lack unity of invention because they lack a common utility that is based upon a common feature or combination of features lacking from the prior art. In the correspondence filed 24 May of 2005, Applicant asserts that SEQ ID NOs: 2, 4, 6 and 8 are alternate splicing forms of a common protein. The common features of these four different sequences do not serve as a unifying feature that distinguishes them as a group from the prior art because the amino acid sequence presented in SEQ ID NO:2 of the Conklin patent (6,020,163) is as similar to any one of those four sequences as they are to each other.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6) Claims 1 to 4, 7 to 9 and 11 are rejected under 35 U.S.C. § 101 because they are drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein identified therein as "$OBPII_{a\beta}$" and the protein encoded thereby. The evidence presented in the instant specification, in conjunction with the Conklin patent, supports a conclusion that the amino acid sequence presented in SEQ ID NO:4 of the instant application corresponds to a human protein that is a member of the lipocalin family. The text beginning on line 11 in column 1 of the Conklin patent indicates that "[l]ipocalins are small secreted proteins that are believed to be involved in the transport of small, hydrophobic molecules". The instant specification appears to assert that SEQ ID NO:4 corresponds to the amino acid sequence of a lipocalin that

functions as an odorant binding protein, based upon its structure and pattern of expression. The probability that SEQ ID NO:4 of the instant application is the amino acid sequence of a human odorant binding protein belonging to the lipocalin family is not in question. However, the claimed invention lacks utility in currently available form because the instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder of physiological process which one would wish to manipulate for a desired clinical effect.

It is clear from the instant specification that the receptor protein described therein is what is termed an "orphan" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins, but its precise function has yet to be determined. Whereas the claimed protein is, in all probability, a lipid binding protein, one would not reasonably conclude that it binds to all lipid molecules, and the instant specification fails to identify that lipid or family of lipids to which the claimed protein binds. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility in modulating the biological activities of those compounds to which it binds. This further characterization, however, is part of the act of invention and until it has been undertaken Applicant's claimed invention is incomplete. Whereas one could readily employ a putative odorant binding protein of the instant invention in an assay to identify ligands thereto the information obtained thereby would be of little use until one discovers the identity of those physiological processes moderated by those ligands. Because the instant specification has failed to credibly identify a specific physiological process which has been shown to

be influenced by the action of a lipid that is bound by a putative odorant binding protein of the instant invention an artisan would have no way of predicting what effects the administration of that odorant binding protein to an organism would have. If one can not predict the effects that the administration of a putative odorant binding protein of the instant invention is going to have on an organism then it is unclear as to what practical benefit is derived by the public from the identification of that protein.

The text at the bottom of page 5 of the instant specification states that a protein of the instant invention "is capable of binding a hydrophobic ligand and in particular odorous molecules, preferably pheromones" and "a receptor". The instant specification, however, fails to identify a single specific compound or receptor that has been shown to bind to the claimed protein. Further, a protein of the instant invention is of human origin, and neither the instant specification nor the prior art of record has identified any compound that functions as a human pheromone.

The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. § 101, which requires that

an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", " [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", " [i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that a protein of the instant invention is associated in any way with "cells of cancerous origin, and mainly breast, uterine, ovarian and lung cancers", as asserted by the text in lines 15 to 18 on page 11 of the instant specification or that they bind to a specific steroid hormone involved in cancer progression, as asserted on page 19 therein. The assertion on page 21 that a protein of the instant invention can be employed "in a process for controlling the volatilization of an odorant" is not a specific assertion because the identity of the odorant or class of odorants is not disclosed and, therefore, the consequence of controlling the volatilization of that odorant has yet to be discovered. Until some actual and specific significance can be attributed to the protein identified in the specification as "$OBPII_{a\beta}$", or the gene encoding it, the instant invention is incomplete. The protein encoded by a DNA of the instant invention is a compound known to be structurally analogous to proteins which are known in the art as lipid binding proteins. In the absence of a knowledge of the natural ligands or

biological significance of this protein, there is no immediately obvious patentable use for it. To employ a protein of the instant invention in the identification of substances which bind thereto is clearly to use it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for "$OBPII_{a\beta}$" then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7) Claims 1 to 4, 7 to 9 and 11 are rejected under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. § 101.

8) Claims 2 and 4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. These claims encompass subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims expressly encompass "a variant of a polypeptide" comprising SEQ ID NO:4. The text beginning on line 5 of page 4 of the instant specification states that "[t]he term "variant polypeptide" will be intended to mean all the mutated polypeptides which may exist naturally, in particular in humans, and which correspond in particular to truncations,

substitutions, deletions and/or additions of amino acid residues". The instant specification, however, does not describe even a single protein that is a variant of a human protein comprising the amino acid sequence presented in SEQ ID NO:4 of the instant application. Whereas the instant specification discloses three splicing alternate forms of SEQ ID NO:4, these are not variants of SEQ ID NO:4 as that term is defined in the instant specification. In the decision of *The Regents of the University of California v. Eli Lilly and Company,* 43 USPQ2d 1398 (CAFC 1997), the court held that:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc. , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel , 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Whereas the instant specification provides a detailed description of a number of isolated DNAs encoding particular putative odorant binding proteins having very specific physical and structural properties, the instant specification does not provide a structural

formula which is definitive of the genus of proteins encompassed by the term "variant" as applied to SEQ ID NO:4. Whereas the instant specification may identify some properties which are common to all odorant binding proteins it does not identify those particular features that distinguish a "variant" of SEQ ID NO:4 from other members of the liipcalin protein family.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9) Claims 3, 4, 7 to 9 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9.1) Claim 3 is vague and indefinite because it is unclear what additional material limitations are placed upon the claimed polypeptide by the presence of the limitation "and named $OBPII_{a\beta}$". This claim is also vague and indefinite because the metes and bounds of the limitation "corresponding to" are unclear. A polypeptide can "have" a referenced sequence or it can "comprise" that sequence, but it is unclear how it can "correspond" to that sequence.

9.2) Claim 4 is vague and indefinite because there is no antecedent basis for "the" Gly-Thr-Trp-Tyr domain.

9.3) Claim 7 is indefinite because it recites a series of progressively narrower values for a single element within the claim. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the

metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 7 recites the broad recitation "at least consecutive nucleotides", and the claim also recites "21 consecutive nucleotides" and "30 consecutive nucleotides" which are progressively narrower statements of the range/limitation. Claims 8, 9 and 11 are indefinite in so far a they depend from claim 7 for this element.

9.4) Claim 8 is vague because it is unclear how the limitation "a radioactive compound or a nonradioactive compound" differs from the limitation "a compound".

9.5) Claims 9 and 11 provide for the use of a polynucleotide of the instant invention as a probe or in a method of treating, but, since the claims do not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 9 and 11 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper

definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10) Claims 2, 4 and 7 to 9 are rejected under 35 U.S.C. 102(e) as being anticipated by the Conklin patent (6,020,163). The Conklin patent described an isolated nucleic acid encoding a lipocalin polypeptide comprising the amino acid sequence presented in SEQ ID NO:2 therein, and the protein encoded thereby. The amino acid sequence presented in SEQ ID NO:2 of Conklin comprises a sequence that is identical to 119 out of the 146 amino acids presented in SEQ ID NO:4 of the instant application and comprised a plurality of fragments at least 15 amino acids in length that are identical to corresponding regions of SEQ ID NO:4. The nucleotide sequence presented in SEQ ID NO:1 of Conklin contains numerous stretches of 15 or more bases that are identical to regions of SEQ ID NO:5 of the instant application, including at least the first 24 bases of the coding region. Example 2 of Conklin described a labeled probe comprising that first 24 bases from SEQ ID NO:1

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John D. Ulm whose telephone number is (571) 272-0880. The examiner can normally be reached on 9:00AM to 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JOHN ULM
PRIMARY EXAMINER
GROUP 1800